

ISIS-3070

PATENT

Please cancel claims 19, 22, 28, 29, 30, 35, 36, 37, 42, 43, 44, 49, 50, and 51, without prejudice.

Claims 15, 21, 23, 24, 25, 32, 39, and 46 have been amended as follows.

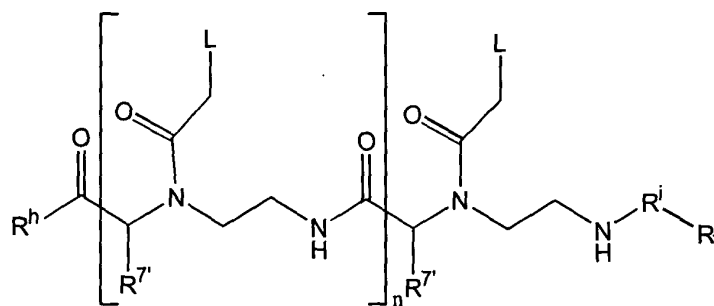
15. A method of modulating cellular uptake and distribution of a peptide nucleic acid comprising the steps of:

- (a) derivatizing a backbone position of said peptide nucleic acid; and
(b) conjugating the derivatized peptide nucleic acid of step (a) with a group selected from alkyl, lipid, and steroid.

21. A method of modulating cellular uptake and distribution of a peptide nucleic acid comprising the steps of:

- (a) conjugating said peptide nucleic acid with a group selected from alkyl, lipid, and steroid; and
(b) introducing the conjugated peptide nucleic acid of step (a) into liposomes.

23. A composition comprising a peptide nucleic acid having formula:



wherein:

each L is, independently, a naturally-occurring nucleobase or a non-naturally-occurring nucleobase;

each R⁷ is hydrogen or the side chain of a naturally-occurring or non-naturally-occurring amino acid, at least one R⁷ being the side chain of a naturally-occurring or non-naturally-occurring amino acid;

R^h is OH, NH_2 , or $NHLysNH_2$.

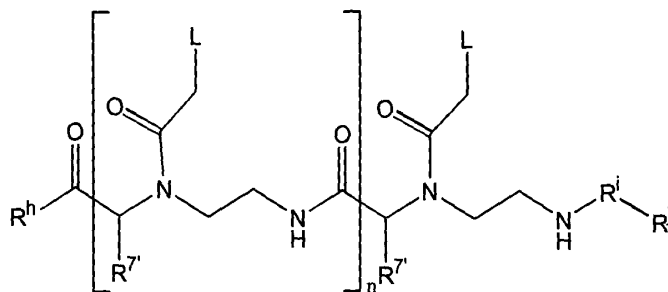
each of Rⁱ and R^j is, independently, a group selected from alkyl, lipid, and steroid; or Rⁱ and R^j, together, are a group selected from alkyl, lipid and steroid; and

n is an integer from 1 to 30;

and at least one pharmaceutically acceptable carrier, binder, thickener, diluent, buffer, preservative or surface active agent.

24. A composition comprising a peptide nucleic acid incorporated into a liposome, said peptide nucleic acid having formula:

3 control



wherein:

each L is, independently, a naturally-occurring nucleobase or a non-naturally-occurring nucleobase;

each R⁷ is hydrogen or the side chain of a naturally-occurring or non-naturally-occurring amino acid;

R^h is OH , NH_2 , or $NHLysNH_2$.

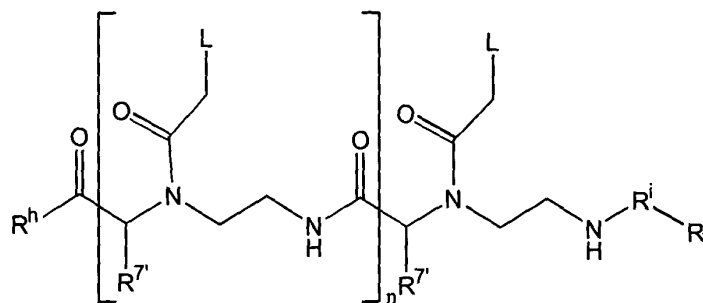
each of Rⁱ and R^j is, independently, a group selected from alkyl, lipid, and steroid; or Rⁱ and R^j, together, are a group selected from alkyl, lipid and steroid; and

n is an integer from 1 to 30;

and at least one pharmaceutically acceptable carrier, binder, thickener, diluent, buffer, preservative or surface active agent.

25. A method of modulating cellular uptake and distribution of a peptide nucleic acid in a cell or tissue comprising administering to the cell or tissue a peptide nucleic acid having formula:

D³ cont'd



wherein:

each L is, independently, a naturally-occurring nucleobase or a non-naturally-occurring nucleobase;

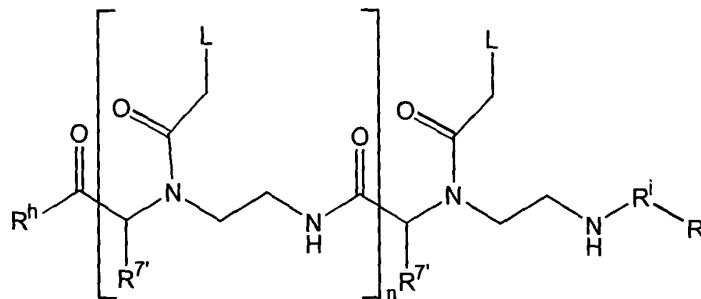
each R⁷ is hydrogen or the side chain of a naturally-occurring or non-naturally-occurring amino acid, at least one R⁷ being the side chain of a naturally-occurring or non-naturally-occurring amino acid;

R^h is OH, NH_2 , or $NHLysNH_2$:

each of Rⁱ and R^j is, independently, a group selected from alkyl, lipid, and steroid; or Rⁱ and R^j, together, are a group selected from alkyl, lipid, and steroid; and

n is an integer from 1 to 30.

32. A method of modulating cellular uptake and distribution of a peptide nucleic acid in a cell or tissue comprising administering to the cell or tissue a composition comprising a peptide nucleic acid incorporated into a liposome, said peptide nucleic acid having formula:



wherein:

each L is, independently, a naturally-occurring nucleobase or a non-naturally-occurring nucleobase;

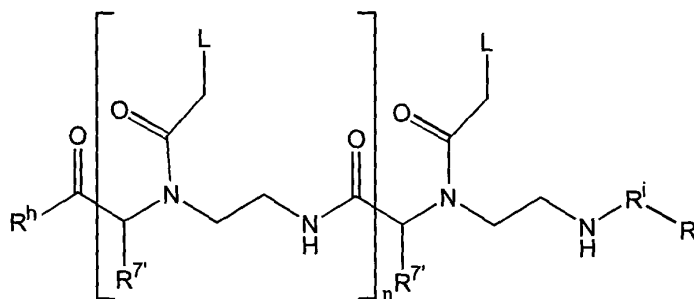
each R⁷ is hydrogen or the side chain of a naturally-occurring or non-naturally-occurring amino acid;

R^h is OH, NH_2 , or $NH\text{Lys}NH_2$;

each of Rⁱ and R^j is, independently, a group selected from alkyl, lipid, and steroid; or Rⁱ and R^j, together, are a group selected from alkyl, lipid, and steroid; and

n is an integer from 1 to 30.

39. A method of modulating gene expression in an animal comprising administering to the animal a therapeutically effective amount of a peptide nucleic acid of formula:



wherein:

each L is, independently, a naturally-occurring nucleobase or a non-naturally-occurring nucleobase;

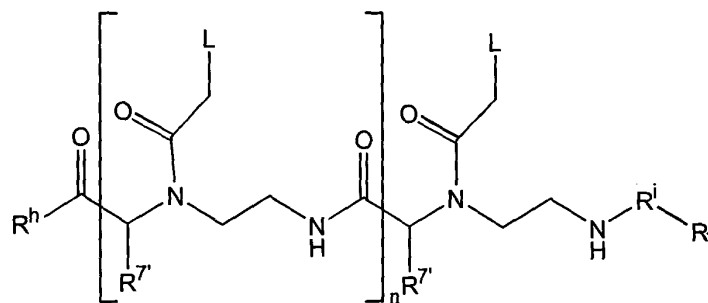
each R⁷ is hydrogen or the side chain of a naturally-occurring or non-naturally-occurring amino acid, at least one R⁷ being the side chain of a naturally-occurring or non-naturally-occurring amino acid;

R^h is OH, NH_2 , or $NHLysNH_2$.

D⁵ control

each of R^i and R^j is, independently, a group selected from alkyl, lipid, and steroid; or R^i and R^j , together, are a group selected from alkyl, lipid, and steroid; and
 n is an integer from 1 to 30.

46. A method of modulating gene expression in an animal comprising administering to the animal a therapeutically effective amount of a composition comprising a peptide nucleic acid incorporated into a liposome, said peptide nucleic acid having formula:



wherein:

each L is, independently, a naturally-occurring nucleobase or a non-naturally-occurring nucleobase;

each R^7 is hydrogen or the side chain of a naturally-occurring or non-naturally-occurring amino acid;

R^h is OH , NH_2 , or $NH-LysNH_2$;

each of R^i and R^j is, independently, a group selected from alkyl, lipid, and steroid; or R^i and R^j , together, are a group selected from alkyl, lipid, and steroid; and

n is an integer from 1 to 30.

REMARKS

Claims 15-52 are pending in this application. Claims 15, 21, 23, 24, 25, 32, 39, and 46